

WHAT IS CLAIMED IS:

1. A composition comprising a recombinant polynucleotide that encodes a modified blood clotting factor, wherein the modification comprises a proteolytic cleavage site not normally present in the factor, and wherein the factor is cleaved at the cleavage site when expressed in an animal cell.
2. The composition of claim 1, wherein the blood clotting factor is a functional variant or a functional subsequence of a naturally occurring blood clotting factor.
3. The composition of claim 1, wherein the blood clotting factor is a vitamin K-dependent procoagulent or anticoagulent protein.
4. The composition of claim 3, wherein the vitamin K-dependent procoagulent protein comprises Factor VII, Factor IX or Factor X.
5. The composition of claim 3, wherein the vitamin K-dependent anticoagulent protein comprises protein C.
6. The composition of claim 1, wherein the proteolytic cleavage site is a mammalian amino acid sequence.
7. The composition of claim 1, wherein the proteolytic cleavage site comprises a PACE/furin amino acid sequence, or functional variant thereof.
8. The composition of claim 1, wherein the proteolytic cleavage site comprises a plurality of basic amino acid sequences.
9. The composition of claim 1, wherein the proteolytic cleavage site comprises Arg-Lys-Arg, Arg-Lys-Arg-Arg-Lys-Arg (SEQ ID NO:1) or PRPSRKRR (SEQ ID NO:2) sequence.
10. The composition of claim 1, wherein the proteolytic cleavage site comprises a viral amino acid sequence cleavage site.

11. The composition of claim 10, wherein the viral cleavage site comprises a retroviral protein amino acid sequence.
12. The composition of claim 11, wherein the retroviral protein cleavage site is an envelope polypeptide cleavage site.
13. The composition of claim 4, wherein the proteolytic cleavage site is introduced between amino acids 152 and 153 of Factor VII.
14. The composition of claim 4, wherein the proteolytic cleavage site is introduced between arginine 152 and isoleucine 153 of Factor VII.
15. The composition of claim 1, wherein the animal cell is mammalian.
16. The composition of claim 15, wherein the mammalian cell is human.
17. The composition of claim 2, wherein the functional variant has one or more conservative amino acid substitutions of wild type blood clotting factor.
18. The composition of claim 2, wherein the functional variant comprises a Factor VII having increased activity relative to wild type Factor VII.
19. The composition of claim 2, wherein the functional variant comprises a Factor VII having increased stability *in vivo* relative to wild type Factor VII.
20. The composition of claim 2, wherein the functional variant comprises a Factor VII having decreased immunogenicity relative to wild type Factor VII.
21. The composition of claim 1, wherein the Factor is mammalian.
22. The composition of claim 21, wherein the Factor is primate, canine, feline, porcine, equine or bovine.
23. The composition of claim 22, wherein the primate is human.

24. The composition of claim 1, wherein the recombinant polynucleotide encoding the modified blood clotting factor is operatively linked to a regulatable or tissue specific expression control element.
25. The composition of claim 24, wherein the regulatable or tissue specific expression control element comprises a promoter.
26. The composition of claim 24, wherein the promoter comprises a skeletal muscle actin promoter or a muscle creatine kinase promoter.
27. The composition of claim 24, wherein the tissue-specific expression control element confers expression of the modified blood clotting factor in muscle, liver, kidney or blood vessel endothelium.
28. The composition of claim 24, wherein the regulatable expression control element comprises elongation factor 1 α promoter.
29. The composition of claim 1, further comprising a vector.
30. The composition of claim 29, wherein the vector comprises a vector suitable for introduction into a cell *in vivo*.
31. The composition of claim 30, wherein the vector comprises an adeno-associated virus (AAV), adenovirus, retrovirus, parvovirus, papilloma virus, reovirus, rotavirus or a herpes virus.
32. The composition of claim 30, wherein the vector comprises a plasmid vector.
33. A polypeptide encoded by the recombinant polynucleotide of claim 1.
34. A kit comprising a composition of claim 1 or a polypeptide of claim 33.
35. A kit comprising a composition of claim 1 further including instructions for expressing the modified blood clotting factor *in vitro*, *ex vivo* or *in vivo*.
36. The composition of claims 1 or 33, further comprising a cell.

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50. The method of claim 42, wherein the subject produces inhibitory antibodies that bind to a clotting factor.
51. The method of claim 50, wherein the inhibitory antibodies bind Factor VIII or Factor IX.
52. The method of claim 42, wherein the subject is a mammal.
53. The method of claim 42, wherein the mammal is human.
54. The method of claim 42, wherein the composition is administered by injection or infusion.
55. The method of claim 42, wherein the composition is administered into the portal vein or spleen.
56. A method of decreasing clotting time in a subject in need of decreased clotting time comprising administering to the subject an amount of the composition of claim 1 sufficient to decrease clotting time in the subject.
57. The method of claim 56, wherein the modified blood clotting factor comprises Factor VII, Factor VIII or Factor IX.
58. The method of claim 56, wherein the subject is a mammal.
59. The method of claim 58, wherein the mammal is human.
60. A method of reducing the frequency or severity of bleeding in a subject in need of reduced frequency or severity of bleeding comprising administering to the subject an amount of the composition of claim 1 sufficient to reduce the incidence or severity of a bleeding in the subject.
61. The method of claim 60, wherein the composition comprises Factor VII, Factor VIII or Factor IX.
62. The method of claim 60, wherein the subject is a mammal.
63. The method of claim 62, wherein the mammal is a human.